SMMGP Clinical Update – April 2010

The effect of time spent in treatment and dropout status on rates of convictions, cautions and imprisonment over 5 years in a primary care-led methadone maintenance service.
Oliver P, Keen J, Rowse G, et al. Addiction 2010;105(4):732-739

This cohort study followed people up over 5 years in a primary care clinic for drug dependence in Sheffield between 1999 and 2005. They started with 108 patients and were able to follow 90 people for the full 5 years. The intervention was methadone maintenance treatment (MMT) and the outcomes were criminal conviction and caution rates, and time spent in prison (taken from the Police National Computer).

Overall, the results showed a reduction in the number of convictions and cautions of 10% for each 6 months spent in treatment. Prior to the study 57% received one or more convictions or cautions in the 12 month period prior to the start of treatment. The group that did best were the people in continuous treatment. In total, just under one-third of the cohort went to prison during the 5-year follow up period and again, those in the continuous treatment were much better off with just 2 members getting custodial sentences (9.2%) compared with 53% of the non-continuous group.
The authors conclude that heroin users treated in primary care can maintain a reduction in acquisitive or drug-related crime for periods up to 5 years.

SMMGP comment:
This study avoids the difficulties of self-reporting by using objective measures of criminality and it shows good evidence of effect. This paper doesn't explore the cost-benefit analysis of a reduction in convictions and cautions but it seems clear there is an obvious bonus to society that extends beyond the personal clinical benefit to the individual of providing effective care. And, of course, it is only one facet of the overall benefits of MMT - but it's one that could be particularly pertinent when it comes to defending methadone maintenance therapy in primary care in the austere climate ahead.

There are some interesting wrinkles in this study. Notably, even those who came in and out of treatment still spent 70% of their time in treatment but this didn't translate into reductions in criminality. It does emphasise the need to retain people in treatment on the first attempt. Curiously, those that were discharged for positive reasons did not fare significantly better than those kept in treatment. This suggests they went on to relapse and re-offend. This isn't a mandate to keep people on methadone indefinitely but it does make one chary of attempts to force on people, for political reasons rather than ones based on individual circumstances, hasty and premature reductions to suit an ideological agenda. We need to consider carefully the most effective period for MMT before tapering or detoxification.

Assessment and management of cannabis use disorders in primary care.
Winstock A, Ford C, Witton J. BMJ 2010;340:c1571.

As one might expect the first thing the authors do in this paper is set out the extent of the cannabis question in our society. Some of the issues to consider are: about one-third of adults in the UK have tried cannabis; an estimated 2.5 million people in the UK have used cannabis in the past year; the noughties have seen a shift toward preparations that have more of the psychoactive tetrahydrocannabinol with less of the

anxiolytic cannabinoid; and finally only 6% of those seeking treatment identify cannabis as their major drug of concern. The authors rightly comment that this low level may also reflect lack of awareness of associated harms.

Some of the key areas covered include: the types of problems that cannabis users might present with in primary care; specific questions that could be asked to identify problem users; the psychological and physiological effects of cannabis and management of withdrawal.

Some of the most likely chronic effects include: dependence (affecting 1 in 10 users); subtle cognitive impairment; COPD (chronic obstructive pulmonary disease)**;** and malignancy of the oropharynx. There are some others which are possible, but remain to be clarified, including: dry mouth leading to dental health problems; a possible reduction in female fertility; low birth weight babies with behavioural problems; and last but not least cannabis may well be an independent risk factor for lung cancer.

SMMGP comment:
Perhaps, most importantly, in a climate of concern over politicised meddling in the Advisory Council on the Misuse of Drugs this paper strikes the right tone – cannabis is not the single biggest issue many clinicians will deal with when it comes to addictions. The common public perception is that it is perhaps considerably less harmful than the legal tobacco and alcohol as well as the illicit substances heroin and cocaine. However, adverse effects of cannabis do exist and we recently discussed the Lancet's paper on this exact topic in the Clinical Update (tinyurl.com/UpdateOct09).

This paper takes it a stage further and firmly sets out the risks, and then puts the management in the context of primary care. At SMMGP we should declare a conflict of interest – one of the authors, Dr Chris Ford, is the Clinical Director of SMMGP, but that won't stop us from saying that if you are looking for a single snappy clinical update on cannabis then this article is the place to go. It lays out in pragmatic, practical terms all that will be useful to any practitioners working in primary care.

Pain and continued opioid use in individuals receiving buprenorphine–naloxone for opioid detoxification: Secondary analyses from the Clinical Trials Network.
Potter JS, Chakrabarti A, Catherine P, et al. Journal of substance abuse treatment 2010;38 (S1) S80–S86

This paper presents a secondary analysis of a study that investigated buprenorphine-naloxone (bup-nx) versus clonidine for opioid detoxification. They wanted to look at the extent to which moderate-to-severe pain at baseline predicted treatment success and how much pain predicted days of opioid use at 15 days after detoxification. As an aside the bup-nx proved to be superior to clonidine in the original study but the aim of this paper was to drag out some of the secondary data related to pain.

In order to analyse this they looked at some sub-components of the questionnaire used in the study. This included 2 items related to pain which addressed: severity "How much bodily pain have you had during the past 4 weeks"; and the impact of the pain "During the past 4 weeks, how much did pain interfere with your activities?"

The results were mixed. Curiously, those who entered treatment with moderate-to-severe pain were more likely to complete treatment successfully. However, at the 15 days post-detoxification follow up there was no association between pain and urine drug screen results. Overall, it was noted that increased pain was associated with *more* days of self-reported opioid use.

SMMGP comment:
The introduction to this paper quotes one reference suggesting that rates of pain in treatment settings have been reported as high as 80%. One could argue that this paper represents the sweepings and offcuts from another more solid and robust

study. Secondary analysis has to be treated with caution but this is a neglected topic of some considerable significance and any additional data are welcome.

Overall, although mixed, the results do support the considerable evidence that persistent pain is associated with negative outcomes and it highlights the importance of exploring this area with those in treatment.

It is perhaps too easy for many clinicians to assume that declared pain is drug-seeking behaviour and there are numerous other factors to consider. Opioid-induced hyperalgesia may complicate the picture and users may have fixed ideas over appropriate analgesia. The two questions this study used provide a very limited basis for the research but they might be an excellent place to start for clinicians who want to start integrating these discussions into their practice.

High rates of sustained virological response in hepatitis C virus-infected injecting drug users receiving directly observed therapy with peginterferon alpha-2a (40KD) (PEGASYS) and once-daily ribavirin. *Waizmann M, Ackermann G. Journal of substance abuse treatment 2010;38(4):338-45*

This was a retrospective open-label study in patients with chronic hepatitis C (CHC) infection treated at an outpatient drug dependency department in Germany. They recruited 49 patients and inclusion criteria were that they had to be aged 18 and older, with no previous treatment for hepatitis C and they were stable on methadone or buprenorphine. Their definition of stability was that they were attending the practice daily and receiving psychosocial support. They also had been in treatment for 6 months and preferably had at least 3 months with no other substance use.

Those that were excluded had HIV co-infection and also 'persistent non-adherence to substitution treatment with illicit drug and/or alcohol use'. However, use during treatment was treated as normal and they weren't excluded from continued CHC therapy.

As part of the program 2 weeks before treatment started all the participants were given 20mg citalopram daily. The antiviral treatment consisted of once a week administration of pegylated interferon and a single dose of 800mg ribavarin daily in the clinic. The opiate substitution therapy, the antiviral meds and the citalopram were also given as directly observed therapy (DOT). Overall, sustained virological response (SVR) was achieved in 48 out of 49 patients - 95% with genotype 1/4 and 100% in genotype 2/3 patients.

SMMGP comment:
The title of this paper may not be initially promising to the busy primary care clinician but there is no papering over the widening crack in future health that hepatitis C represents. Overall, we are not detecting enough cases and even in substance misuse services where we do find some we are simply not able to get those we do diagnose into treatment.

This is a retrospective study but there is food for thought in this paper – they did achieve very good levels of sustained viral response. The use of prophylactic antidepressants is an interesting area to explore with what is often perceived, by patients and clinicians, as a challenging treatment regime. Direct observed treatment (DOT) may not be totally alien to a population used to supervised therapy and it does provide a large amount of support for patients. In addition, the participants in this study also had access to a 24-hour support line.

This is all very intensive but may be necessary to get people through treatment and achieve success. It also highlights that there is one thing that treating the estimated 142,000 in England and Wales with hepatitis C won't be and that is cheap. However, given the future burden it represents it is likely to remain cost-effective but it needs a far-sighted health policy that reaches beyond the political short-termism that hobbles the NHS.

A comparison of methadone, buprenorphine and alpha2 adrenergic agonists for opioid detoxification: A mixed treatment comparison meta-analysis. *Meader N. Drug and Alcohol Dependence 2010;108:110–114*

This was a meta-analysis that compared the efficacy of methadone, buprenorphine, clonidine and lofexidine for opioid detoxification.

There were 23 RCTs (a total of 2112 participants) included in the systematic review but only 20 limped into the meta-analysis. The underlying theory of this meta-analysis is that it allows more comparisons because it allows some indirect comparisons – the theory being that if we know the results of A vs B and B vs C then logic dictates something about A vs C.

SMMGP comment:
The bottom line is that buprenorphine and methadone were ranked as the most effective methods. This is telling in that the Cochrane review suggests there is little difference between methadone and the alpha-adrenergic agonists. The mechanics of this clever piece of meta-analysis geekery may be of scant interest to the average jobbing clinician but the findings do reinforce some commonly held clinical views.

It also suggested that buprenorphine may be the most effective but there was no statistically significant difference between methadone and buprenorphine. However, the way the data are crunched suggests that it is likely buprenorphine is better – it works out that buprenorphine is 85% likely to be most effective. While this is handy to know it takes no account of current maintenance therapy and this is likely to remain one of the most critical factors in determining detoxification regimes for many people.

Excessive substance use in bipolar disorder is associated with impaired functioning rather than clinical characteristics, a descriptive study. *Lagerberg TV, Andreassen OA, Ringen PA, et al. BMC Psychiatry 2010. 10:9*

This Norwegian paper aimed to investigate lifetime rates of illicit substance use in bipolar disorder and compare that to the normal population. They recruited 125 patients from both inpatient and outpatient settings from the Oslo area. They assessed them and they defined excessive substance use using DSM criteria.

They found that the rate of lifetime illicit substance use was significantly higher among patients compared to their reference population (OR 3.03 CI=1.9-4.8). They also noted that those with excessive substance use also tended to have poorer educational levels and there was a trend toward higher suicidality rates. There were no differences between current symptom levels or disease course between the two groups.

SMMGP comment:
It is not at all clear why there might be increased substance use in bipolar disorder and some of the suggestions include an increased tendency towards impulsivity and novelty-seeking behaviour.

The total alcohol use disorder rate was 21% but this was at the lower end of normal compared with previous studies in this area. This might have been related to a high number of females in the study or the lower rates of alcohol consumption in Norway. The increased suicidality is noteworthy and the authors felt this was probably related to the excessive substance use. Curiously, stimulant use didn't seem to increase the incidence of psychosis but this could reflect the high frequency in bipolar patients reducing the relative effect.

Older and sicker: changing mortality of drug users in treatment in the North West of England. *Beynon C, McVeigh J, Hurst A, Marr A. International Journal of Drug Policy. 2010 Feb 19.*

This study examined the age at which drug users die and tried to look to see if there was a significant difference between 'drug-related' deaths and 'non-drug-related' deaths according to age. They looked at data from the National Drug Treatment Monitoring System and identified those that died between April 2003 and March 2008. They then received anonymised data from the Office for National Statistics on the cause of death in 504 people.

The median age at death increased significantly from 36.5 in 2003/4 to 41.4 in 2007/8. The odds of someone aged 40 and over dying from non-drug related death were 3.27 the odds of someone aged less than 40 dying from a non-drug related death.

SMMGP comment:
Interestingly, the majority of people in treatment don't die from a drug-related death. Or at least, not a first glance, as in the over 40s only a quarter were registered as drug-related. However, the other three-quarters have a high proportion of illnesses such as hepatitis C, deep vein thrombosis, endocarditis and lung disease. These aren't regarded as drug-related in the official statistics but are almost certainly a consequence of substance misuse.

On one hand it is really good news to see that the median age of death has increased from 2003/4. Then again, it is utterly horrifying that the median age of death of a group of people in England is just 41.4 years.

What should be done about mephedrone?
Winstock A, Marsden J, Mitcheson L. BMJ 2010;340:c1605.

The authors highlight that amphetamine-type stimulants are believed to cause around 100, mostly accidental, deaths each year in the UK. Many deaths involving stimulants involve poly-drug use and it is possible we will never know if the cases of two young men, so widely reported in the media, were specifically related to mephedrone.

They report that typical effects of mephedrone may include (depending on dose): euphoria, increased energy, feelings of empathy, increased libido, tachycardia, headache and teeth grinding. Users may be excitable, hyperactive and talkative with dilated pupils.

The authors report that the ideal public health response is 'hard to judge' but that the 'same commonsense advice' given to any stimulant user could be offered. This includes: advice to avoid regular use to avoid tolerance; not injecting; keeping well-hydrated; avoid using other stimulants, alcohol and depressants at the same time; and to avoid becoming overheated.

SMMGP comment:
What is really needed, as the authors state is 'credible educational and harm reduction advice'. The problem with mephedrone is that while it is reasonable to assume that it will have similar properties to any psychoactive stimulant ultimately we know very little about it. If we go with the assumption it is similar to other psychoactive stimulants then the groups particularly likely to run into problems with it are those with pre-existing mental health issues, cardiac or neurological problems.

Mixing it up with other drugs and alcohol is likely to increase the risk of a sympathomimetic toxidrome. But ultimately, the problem is we don't know and one of the challenges is a political 'solution', fuelled by the media, that will move into this vacuum.

Adam Winstock has also written an article for SMMGP Network Newsletter setting out some of the clinical features and this is available at tinyurl.com/network29

Anthrax infection in drug users. *Booth MG, Hood J, Brooks TJG, Hart A. Lancet 2010;375:1345-6.*

This letter in the Lancet sets out the current situation with anthrax infection in heroin users in Scotland. At the time of writing there had been 31 cases of infection with 11 deaths in Scotland and with two deaths in England now recorded.

These cases of anthrax haven't presented with the classic features of anthrax in its cutaneous, inhalational or gastrointestional forms. It has been rather variable with three having intracranial or subarachnoid haemorrhage and anthrax bacilli in their blood. They died rapidly in the late stages of disseminated anthrax. The majority have had atypical but severe soft tissue infections. Other features have included vague prodromal symptoms or excessive bruising at the injection site. They typically look very unwell and are tachycardic and shut down (though BP is maintained).

They also commented on the biphasic nature of the disease with several patients apparently stabilising, or even starting to recover, before a rapid and terminal decline which has been 'profoundly unresponsive' to any supportive treatment.

SMMGP comment:
Anthrax can be added to the depressingly long list of infections, sometimes exotic, that injecting drug users risk through continued use.

One of the key features to watch for seems to be atypical and severe soft tissue infections but given the range of problems the main strategy that can be suggested to clinicians is to simply remain aware, informed and vigilant. There is more information available from the HPA where there are interim clinical guidelines for the management of suspected drug users and there is a page of resources at the HPA Scotland website (tinyurl.com/HPAanthrax).

Limited offer to SMMGP members

After the success of the last Clinical Update, which was done in collaboration with the British Psychological Society, the NTA has offered us some copies of the limited-run NTA/BPS publication:

'Psychosocial interventions for drug misuse: a framework and toolkit for implementing NICE-recommended treatment interventions'

to send out to the first 100 people who write in requesting one.

The toolkit "*aims to help drugs workers make better use of 'talking therapies' to support drug misusers overcoming dependency*".

Please send an email to: elsa.browne@nta-nhs.org.uk with **Free copy of Psychosocial Toolkit** in the subject line - and include a postal address - for your chance to receive one free copy.

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